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121 be concluded that there exists no specific tissue alteration which alone may be considered pathognomonic of a single deficiency state: the deficiency must be characterised by all of the clinical signs and symptoms proven to result from a nutritional defect.

● 146 In regard to the Miskito Indians no cases of vitamin deficiency were observed, either by the use of the unproven criteria advocated by Kruse[81] or by the strict clinical evaluation of the subject. Marasmus and malnutrition were observed in infants suffering from diarrhoea, dysentery, or who were abandoned and deprived of food. But other than this finding, little can be said in favor of malnutrition. This becomes obvious in view of the foods these people consume: fruits in season and meats would militate against malnutrition. The people are generally robust and well built regardless of their food habits and while they eat only when hungry, without regularity, it must be admitted that such a method cannot be nutritionally unsound. At Waspook where large quantities of meat and vegetables are consumed the year round, eye lesions often ascribed to ariboflavinosis were commn but the local trader would generally assure a cure by selling dark glasses. The eye conditions were most bothersome during the dry seasons and less so during the rainy season.

The brief study of the dietary habits show that the protein intake from animal food is high, that from legumes relatively low. It has been estimated that the Miskito Indian consumes from 150 to 300 gms. daily of protein, 150 gms. of fat and 200 gms. of carbohydrate; these figures vary somewhat but in general the relationship is about the same. Thus the caloric intake is from 2000-3000 calories daily. These are, of course, average figures determined over a period of time, since the Indian often goes withouh a significant food intake for periods of several days to a week. Except for the fact that the diet of the children may be somewhat low in calcium, there appears to be no dietary deficiencies among these people.

Some of the commonly consumed foods were analyzed and the results are as follows:

[81] Kruse, H. D. Handbook of Nutrition: medical evaluation of nutrional status. Jour. Amer. Med. Assoc. 1943, 20, 584.

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CERTAIN SPECIFIC NUTRITIONAL FACTORS IN COMMON FOODS 146
(Per 100 Grams portion)

	Salt Na Cl. gms.	*Calcium* gms.	*Iron* gms.	*Thiamine* mg.	*Niacin* mg.	*Ascorbic Acid* mg.
Fish:						
Snook	.301	.016	.0016	.06	3.16	
Bass	.202	.028	.0020	.07	2.10	
Monkey	.112	.010	.0028	.092	4.98	
Parrot	.114	.014	.0020	.09	4.36	
Beef	.120	.017	.0032	.062	5.83	
Coconuts	.192	.020	.0014	.02	.42	
Bananas	.131	.006	Trace	.04	.30	7.0
Avocado	.018	.016	.0010	.05	.80	18.0
Oranges	.009	.024	Trace	.06	.16	52.0
Lemons	.005	.023	Trace	.01	.08	72.0
Grapefruits	?	.020	Trace	.03	.10	64.0
Cheese (semicottage)	?	.164	.002	.04	.08	

The intakes of salt average between 1-2 gms. daily; iron between 7-14 mg.; calcium from 0.4-0.9 gms.; thiamin from 0.5-1.0 mg., and niacin from 10-20 mg. During January, February, March and April, the ascorbic acid consumption is low, approximately 10-15 mg. a day. From May to July there is a slight increase of about 5 mg. more in the dietary, while from August to December the intakes will be from 150-300 mg. daily due to the high consumption of citrus fruits, the high intake during this period affords sufficient protection of health during the subsequent period under a maintenance regime.

Clinical findings as regards nutrition. Anemia is the most prevalent finding among children of the Coco River Basin, and what is amazing is the way children tolerate rather drastic reductions in hemoglobin content. Admittedly, altitude is no problem in this region so that at least there is no demand for an increased oxygen capacity of the blood. On the other hand it is impossible to differentiate, clinically, between children having a blood hemoglobin content of 8.0 gms., and those with 13.0 gms. per 100 gms. of whole blood. Furthermore, if the anemia is improved by the use of iron salts the parents may or may not note a difference in the child's behaviour, clinically the difference cannot be detected except in rare instances. In the more severe anemias children complain of lassitude, fatigue, restlessness and lack of energy.

The primary cause of anemia is the type of diet used in early infancy. The child is placed at the breast as soon after birth as possible and is fed whenever it cries. Irregularity in feeding seems to be of no bother to the parents. However, during teething the mother automatically reduces the number of times a day a child is placed at breast since teeth

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146 853 irritate the nipple and causes discomfort to the mother. It is at this point that considerable supplementary feeding is introduced. It is of interest to note that the teeth begin to make their appearance at about the fourth to fifth month in contrast to the average of six to seven months in the United States. The fact that iron reserves are exhausted at about the third month and that supplemental feeding occurs shortly thereafter is a curious coincidence favoring the child.

[827] The Indians believe that food consumed by the mother produces milk and for this reason the mothers eat often and large quantities of food. The children are fed bananas early in life and even if the iron intake from milk supplemented with bananas amounts to 4 mg. a day, it is insufficient to adequately overcome physiological hemoglobin depletion. Theoretically this would soon be made up by foods rich in iron. This in fact is what is attempted by the natives themselves but the anemia is not generally overcome because just as soon as the children begin crawling outdoors form infestation occurs and a relative anemia may be maintained.

146 For practical field use, hemoglobin determinations were carried out using the Sahli equipment and 100 per cent hemoglobin was computed to indicate 15.6 gm. per cent hemoglobin in blood. For purposes of comparison between hemoglobin levels in Guatemala, Yucatán[52] and the Coco territory of Nicaragua, the averages represented:

Guatemalans (691 cases, Shattuck)	73.3 per cent
Yucatecans (2037 cases, Saunders)	71.9 per cent
(1261 cases, Shattuck)	70.6 per cent
Coco River (100 infants, Pijoán)	55.0 per cent

It is admitted that the method of hemoglobin estimation varied, i, e., Shattuck used the Tellquist method, whereas the Sahli method was used in the Coco study. Regardless of this fact, there was less altitude in the Coco Basin to provoke hemoglobin increases and secondly the incidence of insidious disease seemed greater.

Hemoglobin values in 100 infants (2-3 months old) in Zapuca and Waspam, Coco Basin, Nicaragua.

Number of Infants	*Hemoglobin value*
29	60-70 per cent
48	50-60 per cent
23	40-50 per cent

Another point of difference between this study and the others is that the findings by Shattuck was fairly representative of his territory

[52] Shattuck, G. C. A Medical Survey of Guatemala. Carnegie Institution of Washington. 1938.

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in regards to age groups whereas this one concerned itself with infants where anemia was to be expected. Furthermore Shattuck was able to exclude malaria as a cause of anemia.

Blood smears were examined and the significant findings were a slight achromia and variation in size and shape of the red cells, and microcytosis characteristic of chronic hypochromic microcytic anemia commonly associated with iron deficiency in the body.[51] So far then in infants and early childhood the prevalent deficiency is an iron lack which was found to be so not necessarily on clinical evidence but on laboratory investigation. .

Hypochromic anemia. The relatively low iron content of milk (1.8-2.3 mg. 1 liter Fe) [53] accounts for the presence of anemia in early infancy and subsequently a diet, early in life, not rich in iron may not overcome the depleted iron reserves. To this is added the anemia sustained by the effects of infection and intestinal parasitism. Since the more severe anemias occur in those subjects with hookworm disease an iron balance study was undertaken.

Balance study of four subjects with Necator Americanus infestation: Since the demonstration by Stiles,[54] Harris, [55] and others, that hookworm infestation in the United States in associated with anemia, the relationship of cause and effect the syndrome has received attention

Recently Rhoads, Castle, Payne and Lawson[56] have advanced the view that the anemia resulting from hookworm infestation is due to blood loss through the bowel. This is based on the fact that the worms with their hooks cause minute hemorrhages in the bowel wall, but they have stated as have other observers[57], [58] that although there is a slow hemapoietic response to iron therapy during infestation a dramatic response to treatment occurs only when it is administered after the removal of the worms. The assumption that this is a blood loss anemia

[53] Peterson, W. H., and Elvehjen, C. A. The Iron Content of Plant and Animal Foods. Jour. Nutrition, 1931, *4*, 419.

[54] Stiles, C. W. Report upon the prevalence and geographic distribution of hookworm disease. U. S. Govt. Print. Off., U. S. Public Health Service Hyg. Lab. Bull., 1903, *10*.

[55] Harris, H. F. Ankylostomiasis, the most common of the serious diseases of the southern part of the United States. Amer. Med. 1902, *4*, 776.

[56] Rhoads, C. P., Castle, W. B., Payne, J. C., and Lawson, H. A. Observations on the etiology and treatment of anemia associated with hookworm infection in Puerto Rico. Medicine, 1934, *13*, 317.

[57] Rotter, W. Ueber die histologischen Veränderungen des Dunndarms bei Ankylostomiasis. Virchows Arch. of path. Anat. 1931, *280*, 587.

[58] Rhoads, C. P., and Castle, W. B. Observations on the etiology and treatment of the anemia of hookworm disease in Porto Rico. Jour. Clin. Invest. 1932, *11*, 809.

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is based on the blood picture, bone marrow examination and on the fact that the effect of iron therapy was moderate until after the removal of the worms. The fact that live extract exerted no particular effect was interpreted by Rhoads and his associates to support their view.

The assumption that blood loss is the cause hookworm anemia is a good one since it is obvious that the worm draws through its gastro-intestinal tract a fairly copious amount of blood. In fact, much of the blood may pass through the worm in an unused condition. On the other hand it is of interest to note that the degree of anemia and the number of worms present in an individual cannot be correlated.[59], [60] Actually it has been found that a small number of parasites can cause a profound anemia. Whipple,[61] furthermore, has found weak hemolytic factors in hookworms which has suggested the chronic effects of a hemolysin.

The morphological characteristics of the blood cells in hookworm anemia are not those found in hemolytic jaundice. There is besides this consideration the report of De Langen[62] which expresses the view that hookworms secrete a substance toxic to bone marrow. It may be that a variety of factors aside from blood loss exist which are responsible for the anemia. So far no one has attempted to determine iron utilization in subjects with hookworm infestation, a feat which today could be studied to advantage with radio active iron. Our studies, however, were carried out using the classical method of iron balance in which certain errors may occur.

The iron balance was performed in four subjects with hookworm infestation. The procedure used was that described by Farrar[63] and the iron assays of food and feces were performed by the method of Pijoan and Elkin.[31] The only hematological inquiry was the hemoglobin determination in order to ascertain the response to various intakes of iron. The subjects were boys, two of them of 8 years of age, one of 10 years and another of 12 years. As far as could be ascertained all

[59] Smillie, W. G. Studies on Hookworm infection in Brazil. Rockefeller Inst. Monograph, 1922, *17*, 46.

[60] Rosenblum, M. B., and Malkowa, M. N. Zur Charakteristik der Anaemia bei Anchylostoma duodenale. Folia Haematol., 1928, *37*, 197.

[61] Whipple, G. H. The presence of a weak hemoglobin in the hookworm and its relation to the anemia of Uncinariasis. J. Expl. Med., 1909, *11*, 331.

[62] De Langen, C. D. Contributions to the toxic origin of the Anaemia and other symptoms with Ankylostomiasis. Trns. 5th Biennial for East. Assn. Trop. Med. London, 1924.

[63] Farrar, G. E. Jr. The determination of iron in biological material. Jour. Biol. Chem., 1935, *110*, 683.

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of them had untreated hookworm infestation of some duration. There was no method at our disposal to accurately determine the degree of infestation. The diet consisted chiefly of milk, bread, cheese, avocado, banan, vitamins and eventually ferrous sulfate supplements. The results are expressed in the following tables.

SUBJECT I

	Intake mg.	*Feces Fe Output* mg.	*Balance* mg.	*Hbg.* %	*Occult Blood in Stools*
1	7.31	7.40	— 0.09	7.4 gms.	None
2	7.42	7.40	— 0.02		None
3	7.21	7.40	— 0.19		None
4	7.46	7.50	— 0.04	7.38 gms.	None
5	7.33	7.31	+ 0.02		None
6	7.37	(*)			
7	7.56	7.49	+ 0.04		Trace
8	8.22	8.31	— 0.09		Trace
9	8.41	8.39	+ 0.02		None
10	8.30	8.30	———		
11	8.60	8.75	— 0.15		Trace
12	8.75	8.62	+ 0.13		None
13	8.80	(*)			
14	8.20	8.31	— 0.11	7.38 gms.	None
15	8.36	8.30	+ 0.06		None
16	8.41	8.46	— 0.05	7.36 gms.	

Total Balance in 16 days — 0.51

* Specimens lost.

SUBJECT II

	Intake mg.	*Feces Fe Output* mg.	*Balance* mg.	*Hbg.* %	*Occult Blood in Stools*
1	11.13	11.15	———		
2	11.20	11.21	— 0.01	6.0 gms.	None
3	10.40	10.38	+ 0.02		Trace
4	10.81	10.58	+ 0.23		None
5	9.68	9.72	— 0.14		None
6	10.41	10.46	— 0.05	5.8 gms.	Trace
7	10.28	10.30	— 0.02		None
8	9.34	9.36	— 0.02		Trace
9	9.82	9.79	+ 0.03		None
10	10.56	10.58	— 0.02		None
11	10.62	10.62	———		Trace

12	10.84	10.83	+ 0.01	6.0 gms.	Trace
13	11.36	11.36	———		None
14	11.42	11.43	— 0.01		None
15	11.41	11.42	— 0.01		None
16	13.64	13.63	+ 0.01	6.12 gms.	None

Total Output Equals Intake Neg. Balance.

SUBJECT III

	Intake mg.	*Feces Fe Output* mg.	*Balance* mg.	*Hbg.* %	*Occult Blood in Stools*
1	18.75	18.76	— 0.01	5.16 gms.	None
2	22.41	21.06	+ 0.35		None
3	19.35	19.37	— 0.02		Trace
4	20.36	20.36	———		None
5	21.10	21.08	+ 0.02		None
6	20.34	20.36	— 0.02		Trace
7	22.10	22.09	+ 0.01		None
8	21.15	20.15	———		None
9	18.98	18.96	+ 0.02		None
10	19.26	19.25	+ 0.01		None
11	19.34	19.34	———		None
12	19.71	20.74	— 0.03	5.80 gms.	Trace
13	19.24	19.23	+ 0.01		None
14	19.49	19.47	+ 0.02		None
15	20.10	20.10	———		None
16	20.18	20.17	+ 0.01	6.0 gms.	None

Total Balance 0.38 mg.
0.0237 mg. per day

SUBJECT IV

Supplemental Iron Given (given 75 mg. $FeSO_4$ = 27.5 mg. Fe)

	Intake mg.	*Feces Fe Output* mg.	*Balance* mg.	*Hbg.* %	*Occult Blood in Stools*
1	36.41	36.38	0.03	7.12 gms.	No
2	37.42	37.39	0.03		tests
3	36.30	36.28	0.02		done
4	38.40	38.31	0.09	7.40 gms.	because
5	44.76	43.57	1.19		of
6	45.71	44.65	1.06		high
7	44.84	43.78	1.06	8.0 gms.	iron
8	44.73	43.66	1.07		intake

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9	45.12	43.11	2.01	
10	43.19	42.13	1.06	9.0 gms.
11	39.38	39.30	0.08	
12	38.40	38.31	0.09	
13	37.41	37.32	0.09	10.5 gms.
14	36.64	36.59	0.05	
15	38.52	38.45	0.07	11.5 gms.

Total Intake 9.11 mg. or 0.57 mg. Fe daily.

Since the amount of iron in urine is negligible and would indicate if anything in favor of negative balance no urinary excretion iron assays were performed. It is obvious from our study that a positive but slight (0.0237 mg.) balance is shown when the consumption of iron is in the neighborhood of 18 mg. iron intake a day, but it is known that during early life iron requirements are considerable and the drains upon the iron stores will then be the greatest. Exhaustion of iron stores takes place during the first year of life when the total blood volume is tripled and the total hemoglobin doubled.[54] A low iron intake at this time will bring about a depletion of the iron reserve. At the age when Necator infestation manifests itself the hemoglobin stores are often low or exhausted. It has been calculated by Heath and Patek that the average annual requirement of a 10 year hold child is about 0.152 grams or 0.04 mg. per day of absorbed iron (derived from a positive balance). It is obvious therefore that the iron utilization of 0.0237 mg. per day is quite insufficient, especially when the body stores are depleted. Thus, in Necator infestation more iron is required, and the administration of supplemental iron (75 mg. $FeSO_4 = 27.5$ Mg. Fe) brings about a positive balance where 0.57 mg. Fe are apparently absorbed daily. From subfindings it seems clear that the anemia of hookworm requires treatment with large doses of iron and it has been the clinical experience of others[56] that improvement takes place only with large doses of iron ammonium citrate and ferrous sulfate. On the other hand the hemoglobin increases 1/2 per cent per day if the worms are first removed.[56] These data presented here lead us to conclude that the explanation of anemia based entirely on blood loss from the bowel is an unsatisfactory one. Even though it may contribute to the anemia of Necator infestation, some other mechanism must play a role in sustaining the anemia. Whether the worms secrete a toxin which affects the hemopoietic system or a substance which forms unassimilable iron salts is a matter of conjecture and requires further inquiry. It has been noted that about fifty per cent of subjects with hookworm infes-

[54] Heath, C. W., and Patek, A. J., Jr. Anemia of iron deficiency. Medicine, 1937, *16*, 267.

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tation have chronic diarrhoea, some have glossitis,[65] occasionally leucopenia and lymphocytosis is observed. Reticulocyte counts usually were under 3 per cent and studies on platelets show them to be within normal limits. These findings indicate some unusual process in Necator hypochromic anemia.

Our own assays of the worms themselves reveal an iron content of only 1-2 mg. Fe per kilogram. It seems unlikely therefore that iron consumption by the worm plays a rôle in the anemia.

WORM INFESTATIONS

Because the writer is not a helminthologist the classification of intestinal parasites is not a complete one and depended considerably on the aid given him by laboratory assistants. However, certain aspects of the subject are intriguing. Sandground[66] has pointed out that the data dealing with intestinal parasites can be collated in such a way as to throw light on the racial origins of some of the Indians and to bear witness to the invasion of Central American countries by alien races. Von Thering according to Sandground had demonstrated the value of testimony from the world of parasitism as an aid to zoogeography and paleozoology. For instance, in recognizing the close affinities between the tapeworms harbored by marsupials in South America and Australia, Zschokke[67] presented evidence of a phylogenetic relationship in their hosts. Metcalf[68] also demonstrated by studies on opalinid ciliates in Amphibia a genetic relationship between frogs of South America and Australia and brought out new facts which tended to corroborate hypotheses in geography dealing with land masses connecting now isolated continents. Using information on the history of certain infectious diseases, and their prevalence in certain races, Williams[69] used the host-parasite association as a means of studying racial relationships among American Indians.

[65] Ashford, B. K., King, W. W., and Gutiérrez, P. Report of the study and treatment of "anemia" in Porto Rico. Bur. Print. and Supplies, San Juan, 1904.

[66] Sandground, J. H. Consideration of relation of host specificity of helminths and other metazoan parasites to phenomena of age resistance and acquired immunity. Parasitology, 1929, *21*, 227-255.

[67] Zschokke, F. Die Darmcestoden der Amerikanischen Beuteltiere. Centralbl. f. Bakteriol. 1904. *36*, 51-62.

[68] Metcalf, M. M. Bull. 120, U. S. Nat. Mus. 1923: Smithsonian Misc. Coll. 1929, *81*, No. 18.

[69] Williams, H. U. The epidemic of the Indian of New England, with remarks on Native American Infections. Johns Hopkins Hosp. Bull. 1909, *20*, 340-349; 1616-1620.